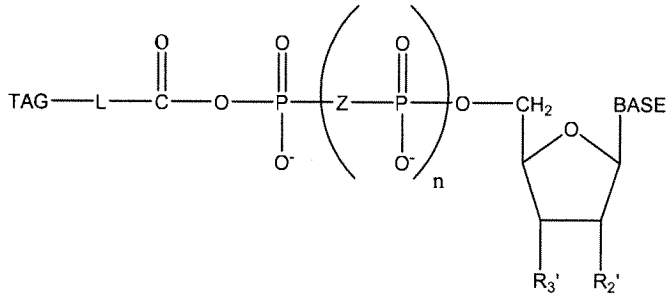
Amendments to the Claims/Listing of Claims

Please amend claims 1-19 and 27 as follows. This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-~~nucleotide~~ **phosphate or phosphonate** probe ~~having~~ **according to claim 28 wherein X is a nucleotide, such that said probe has** the formula:



wherein

BASE is a 5- or 6-membered unsaturated heterocyclic ring comprising from 1 to 3 ring nitrogens, wherein the 5- or 6-membered unsaturated heterocyclic ring is covalently attached through a ring nitrogen to the 1' position of the ribose or deoxy-ribose, wherein the 5- or 6-membered unsaturated heterocyclic ring optionally comprises a 6-membered unsaturated carbocyclic or heterocyclic ring fused thereto, said fused ring comprising from 1 to 2 ring nitrogens, and wherein each carbon position in the BASE may be optionally substituted by a substituent independently selected from the group consisting of -H, -F, -Br, -Cl, $-SCH_3$, -C(O)N(R)(R), -CN, $-NO_2$, -N(R)(R), =O, acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, or $-(CH_2)_mOH$;

$R_{2'}$ and $R_{3'}$ are independently selected from the group consisting of -H, -OH, -F, -Br, -Cl, $-SCH_3$, -C(O)N(R)(R), -CN, $-NO_2$, -N(R)(R), acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, $-(CH_2)_mOH$, or

$-(CH_2)_m$-phenyl where phenyl is optionally substituted with -F, -Br, -Cl, $-SCH_3$, $-C(O)N(R)(R)$, -CN, $-NO_2$, -N(R)(R), acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, $-(CH_2)_mOH$;

n is 0-2;

m is 0 to 6; **and**

TAG_1 ~~**is a detectable label;**~~

~~**each**~~ Z ~~**is independently O, S, NH, or methylene;**~~

and L ~~**is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of -N(R)-, -O-, -S- or -C(R)(R)-, wherein said alkyl or heteroalkyl group optionally includes a carbocyclic or heterocyclic group;**~~

~~**each R is independently H or $-C_{1-6}$-alkyl straight or branched chain, or optionally form an optionally substituted fused carbocyclic or heterocyclic ring structure; and**~~

~~**the carbonyl adjacent to L is bound to a carbon to form an acyl group;**~~

~~**or a pharmaceutically acceptable salt or complex thereof**~~ **are as previously defined**.

2. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe according to claim 1, wherein BASE is a purine.

3. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe according to claim 1, wherein BASE is a pyrimidine.

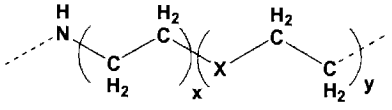
4. (Withdrawn; Currently amended) **[[An]] <u>A tagged</u>** acyl-nucleotide probe according to claim 1, wherein BASE is selected from the group consisting of adenine, thymine, uracil, guanine, cytosine, inosine, 5-bromouracil, 5-fluorouracil, 2-aminopurine, N^6-cyclohexyl adenine, 8-azaguanine, and 5-fluorocytosine.

5. (Withdrawn; Currently amended) **[[An]] <u>A tagged</u>** acyl-nucleotide probe according to claim 4, wherein BASE is selected from the group consisting of adenine, thymine, uracil, guanine, and cytosine.

6. (Withdrawn; Currently amended) **[[An]] <u>A tagged</u>** acyl-nucleotide probe according to claim 1, wherein $R_{2'}$ and $R_{3'}$ are independently H or OH.

7. (Withdrawn; Currently amended) **[[An]] <u>A tagged</u>** acyl-nucleotide probe according to claim 1, wherein $R_{2'}$ and $R_{3'}$ are each OH.

8. (Withdrawn; Currently amended) **[[An]] <u>A tagged</u>** acyl-nucleotide probe according to claim 1, wherein L has the structure:

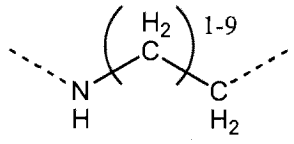


where**<u>in</u>**

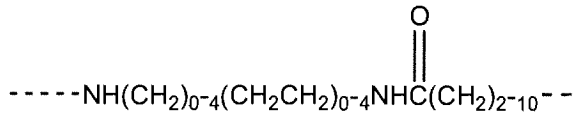
x and y are independently in the range of 0 to 4, and

X is O or CH_2.

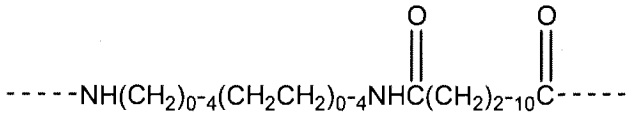
9. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe according to claim 1, wherein L has the structure:



;



; or



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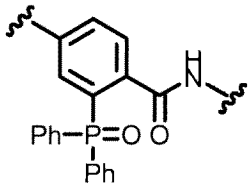
10. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe according to claim 8, wherein L has the structure $-NH(CH_2)_2(OCH_2CH_2)_{1-4}-$.

11. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe according to claim 1, wherein L comprises a triazole moiety.

12. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl nucleotide probe according to claim 1, wherein L comprises the following moiety:



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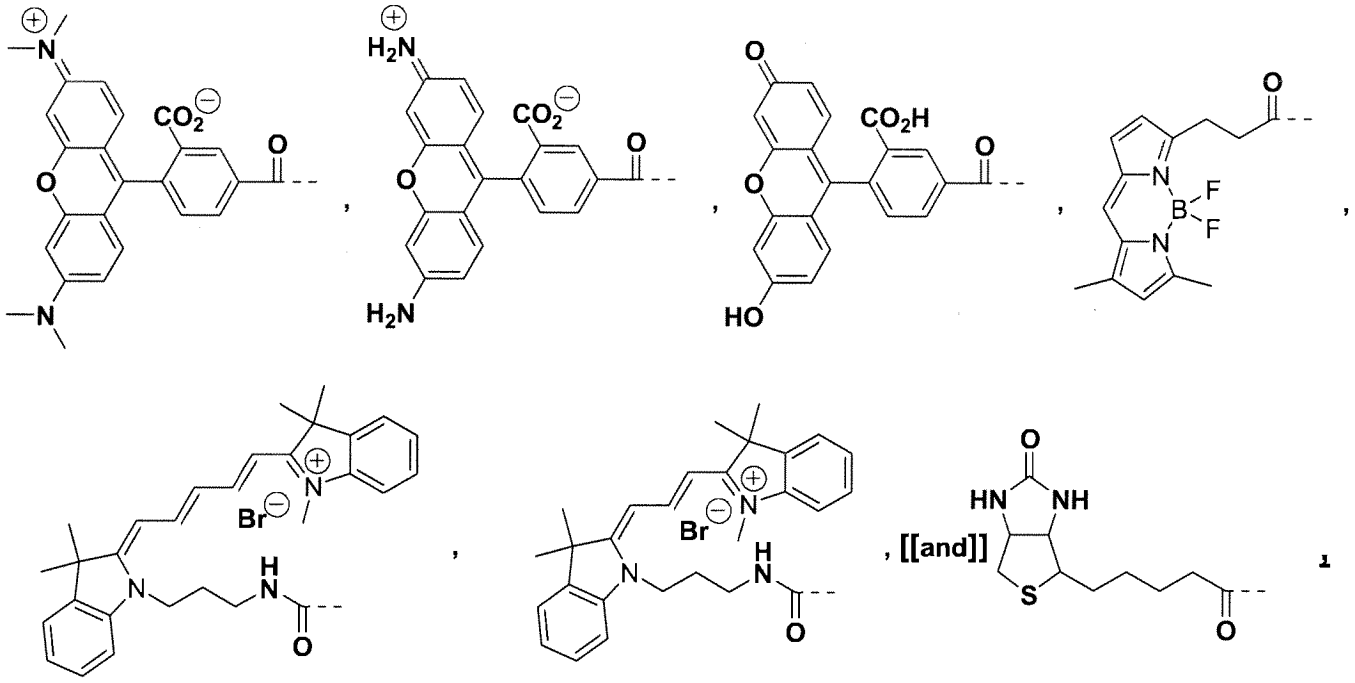
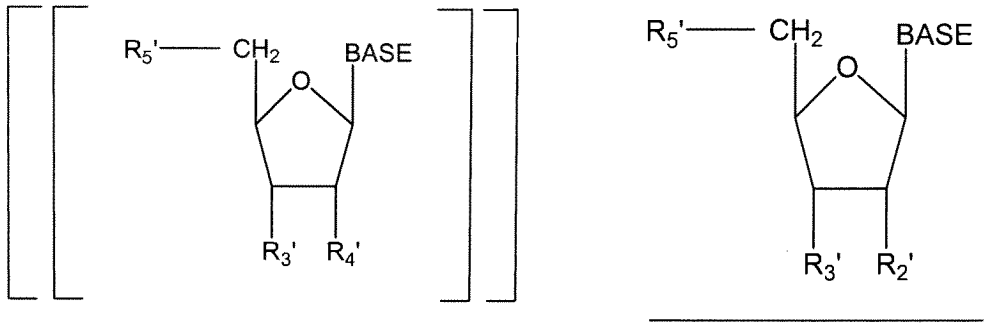
13. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe according to claim 1, wherein the TAG is selected from the group consisting of:



and dethiobiotin; wherein 5-substituted carboxyrhodamine or 5-substituted carboxyfluorescein may be replaced with 6-carboxyrhodamine or 6-carboxyfluorescein, or with a mixture of 5- and 6- substituted carboxyrhodamine or carboxyfluorescein.

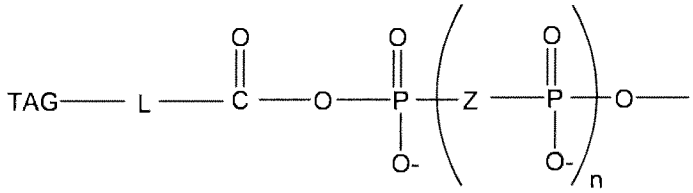
14. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-~~nucleotide~~ **phosphate or phosphonate** probe ~~having~~ **according to claim 28 wherein X is a nucleotide, such that said probe has** the structure:



wherein

BASE is a 5- or 6-membered unsaturated heterocyclic ring comprising from 1 to 3 ring nitrogens, wherein the 5- or 6-membered unsaturated heterocyclic ring is covalently attached through a ring nitrogen to the 1' position of the ribose or deoxy-ribose, wherein the 5- or 6-membered unsaturated heterocyclic ring optionally comprises a 6-membered unsaturated carbocyclic or heterocyclic ring fused thereto, said fused ring comprising from 1 to 2 ring nitrogens, and wherein each carbon position in the BASE may be optionally substituted by a substituent independently selected from the group consisting of -H, -F, -Br, -Cl, $-SCH_3$, -C(O)N(R)(R), -CN, $-NO_2$, -N(R)(R), =O, acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, or $-(CH_2)_mOH$;

one of $R_{2'}$ and $R_{3'}$ and $R_{5'}$ has the following structure:



and the other two of $R_{2'}$ and $R_{3'}$ and $R_{5'}$ are independently selected from the group consisting of -H, -OH, -F, -Br, -Cl, $-SCH_3$, -C(O)N(R)(R), -CN, $-NO_2$, -N(R)(R), acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, $-(CH_2)_mOH$, or $-(CH_2)_m$-phenyl where phenyl is optionally substituted with -F, -Br, -Cl, $-SCH_3$, -C(O)N(R)(R), -CN, $-NO_2$, -N(R)(R), acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, $-(CH_2)_mOH$;

n is 0-2;

m is 0 to 6; **and**

TAG, ~~**is a detectable label;**~~

~~**each**~~ Z ~~**is independently O, S, NH, or methylene;**~~

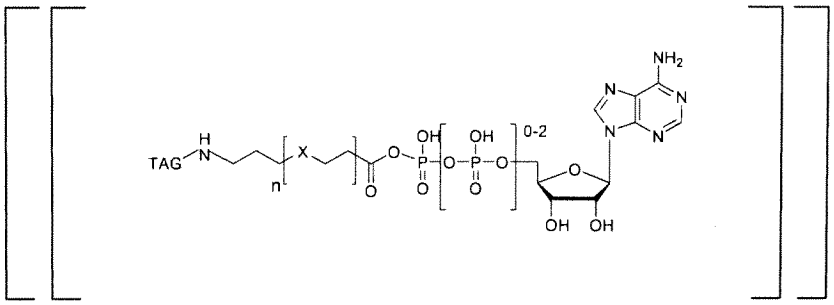
and L ~~**is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of -N(R)-, -O-, -S- or -C(R)(R)-, wherein said alkyl or heteroalkyl group optionally includes a carbocyclic or heterocyclic group;**~~

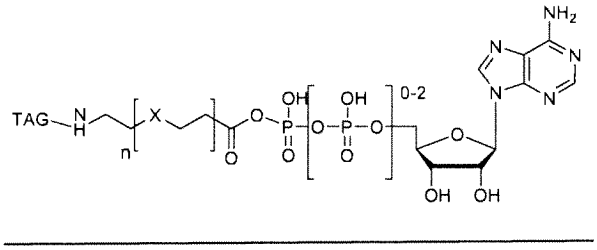
~~**each R is independently H or $-C_{1-6}$ alkyl straight or branched chain, or optionally form an optionally substituted fused carbocyclic or heterocyclic ring structure; and**~~

~~**the carbonyl adjacent to L is bound to a carbon to form an acyl group;**~~

~~**or a pharmaceutically acceptable salt or complex thereof**~~ **are as previously defined**.

15. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe having the structure:





wherein

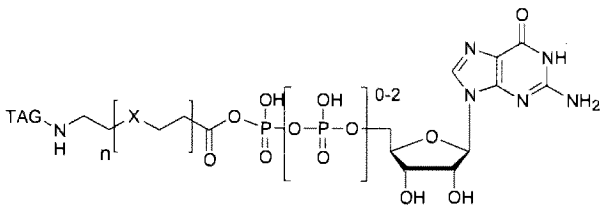
n is 1-4;

X is O or CH_2; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

16. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe having the structure:



wherein

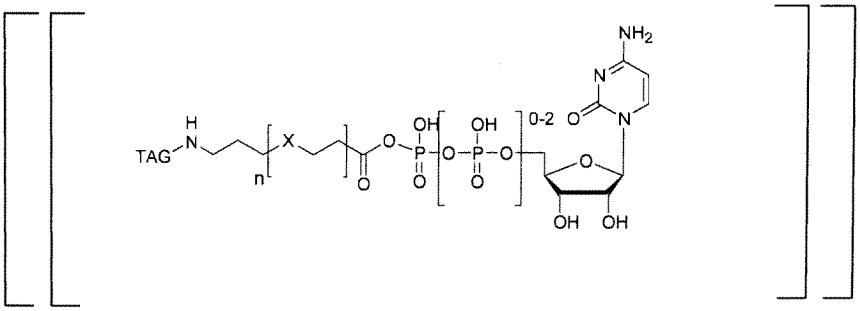
n is 1-4;

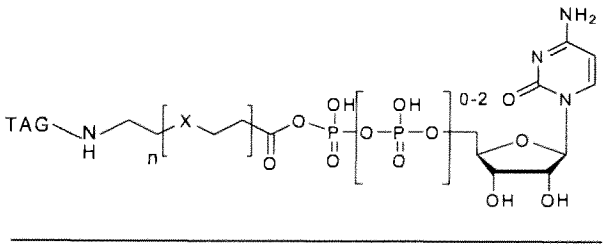
X is O or CH_2; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

17. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe having the structure:





wherein

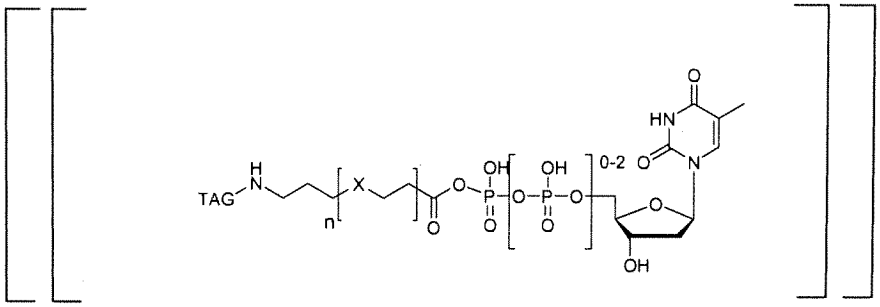
n is 1-4;

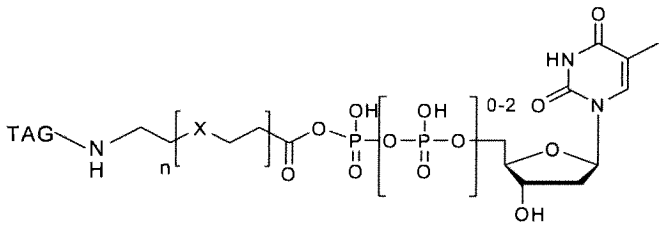
X is O or CH_2; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

18. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe having the structure:





wherein

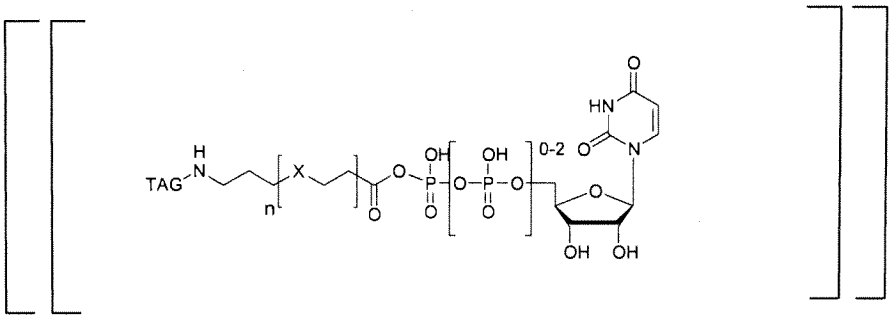
n is 1-4;

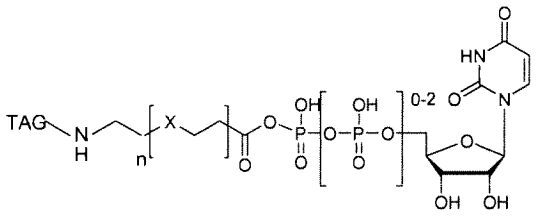
X is O or CH_2; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

19. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe having the structure:





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wherein

n is 1-4;

X is O or CH_2; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

20. (Withdrawn) A method for determining the enzyme profile of one or more target proteins in a complex protein mixture, employing one or more probes comprising a nucleotide covalently bound through the terminal phosphate of a 5' mono- di- or tri-phosphate to an acyl group, which is further covalently bound to a TAG via a linker moiety "L", wherein said acyl group forms an adduct with said target protein(s) when said probe is bound to said target protein(s), said method comprising:

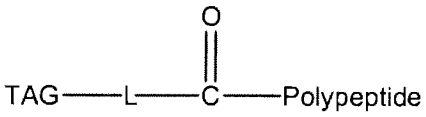
combining in a reaction medium said probe(s) and said complex protein mixture under conditions of reaction of said probe(s) with said nucleotide binding protein(s), whereby a conjugate of said probe(s) and said target protein(s) is formed; and

determining said enzyme profile by generating a signal from one or more conjugates formed thereby;

wherein said probe(s) are selected from the nucleotide binding protein-directed probes of one of claims 1-18.

21. (Withdrawn) A method according to Claim 20, wherein said probe binds to a plurality of target proteins.

22. (Withdrawn) A composition comprising a purified labeled polypeptide having the structure:



wherein

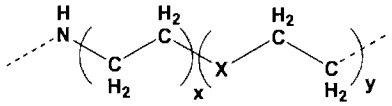
TAG is a detectable label or a solid support;

L is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of -N(R)-, -O-, -S- or -C(R)(R)-, wherein said alkyl or heteroalkyl optionally includes a carbocyclic or heterocyclic group;

the carbonyl adjacent to L is bound to a carbon to form an acyl group; and

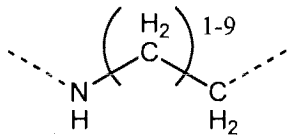
the acyl group is covalently attached through an amide, ester, or thioester linkage to a Polypeptide amino acid residue.

23. (Withdrawn) A composition according to claim 22, wherein L has the structure:

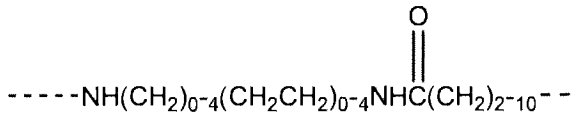


where x and y are independently in the range of 0 to 4, and X is O or CH_2.

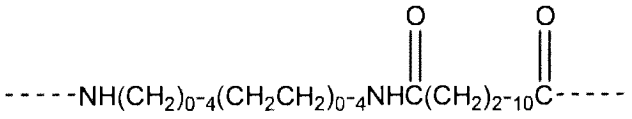
24. (Withdrawn) A composition according to claim 22, wherein L has the structure:



;



; or



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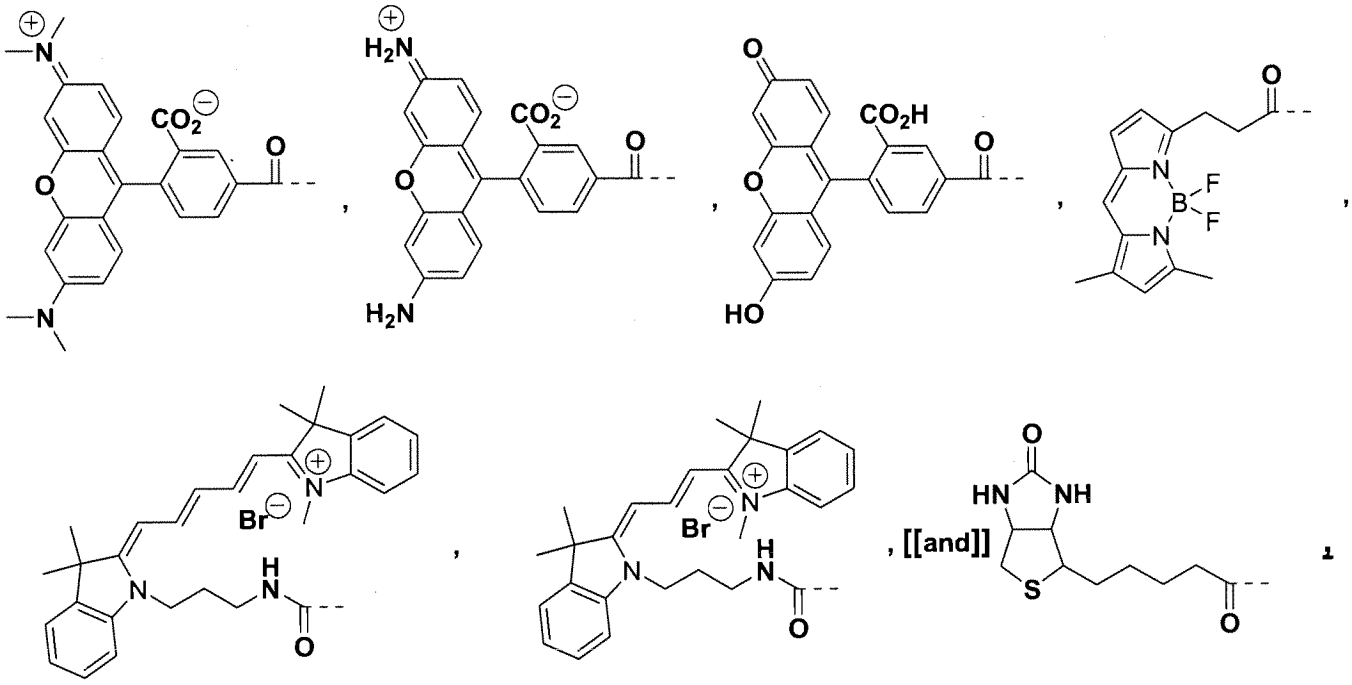
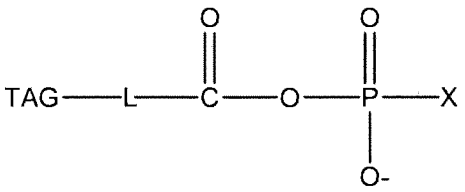
25. (Withdrawn) A composition according to claim 20, wherein L has the structure $-NH(CH_2)_2(OCH_2CH_2)_{1-4}-$.

26. (Withdrawn; Currently amended) A composition according to claim 20, wherein the TAG is selected form the group consisting of:



and dethiobiotin; wherein 5-substituted carboxyrhodamine or 5-substituted carboxyfluorescein may be replaced with 6-carboxyrhodamine or 6-carboxyfluorescein, or with a mixture of 5- and 6- substituted carboxyrhodamine or carboxyfluorescein.

27. (Currently amended) A tagged acyl phosphate or phosphonate probe having the formula:



wherein

X is an affinity moiety for directing the binding of said TAPP to one or more target proteins linked to the ~~**phophate**~~ **phosphate** through an oxygen or carbon;

TAG is a detectable label;

L is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of -N(R)-, -O-, -S- or -C(R)(R)-, wherein said alkyl or heteroalkyl group optionally includes a carbocyclic or heterocyclic group;

each R is independently H or -C_{1-6} alkyl straight or branched chain, or optionally form an optionally substituted fused carbocyclic or heterocyclic ring structure; and

the carbonyl adjacent to L is bound to a carbon to form an acyl group;

or a pharmaceutically acceptable salt or complex thereof.

28. (Original) The tagged acyl phosphate probe of claim 27, wherein X is selected from the group consisting of a nucleotide, nucleotide analogue, optionally substituted naphthyl group, small molecule, steroid, peptide hormone, enzyme cofactor, vitamin, enzyme substrate, lipid, prostaglandin, or receptor ligand.

29. (Withdrawn) A method of synthesizing a tagged acyl phosphate or phosphonate probe, comprising:

contacting a detectable label comprising a linking group L terminating in a carboxyl group, with a nucleotide or nucleotide analogue comprising a 5'-linked phosphate comprising an available -OH group in the presence of diisopropylcarbodiimide or isobutyl chloroformate and triethylamine to form said tagged acyl phosphate or phosphonate probe; and

purifying said probe.